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L7 and antibody

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<u>L8</u>	L7 and antibody	30	<u>L8</u>
<u>L7</u>	((424/246.1)!.CCLS.)	46	<u>L7</u>
<u>L6</u>	L5 and bacillus	4	<u>L6</u>
<u>L5</u>	s ea1	253	<u>L5</u>
<u>L4</u>	L3 and ea1	0	<u>L4</u>
<u>L3</u>	L2 and anthracis	79	<u>L3</u>
<u>L2</u>	L1 and antibodies	227	<u>L2</u>
<u>L1</u>	anthrax	419	<u>L1</u>

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Term:

L2 and anthracis

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<u>L6</u>	L5 and bacillus	4	<u>L6</u>
<u>L5</u>	s ea1	253	<u>L5</u>
<u>L4</u>	L3 and ea1	0	<u>L4</u>
<u>L3</u>	L2 and anthracis	79	<u>L3</u>
<u>L2</u>	L1 and antibodies	227	<u>L2</u>
<u>L1</u>	anthrax	419	<u>L1</u>

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L3: Entry 43 of 79

File: USPT

Jul 31, 2001

US-PAT-NO: 6267966

DOCUMENT-IDENTIFIER: US 6267966 B1

TITLE: Vaccine production of the Bacillus anthracis protective antigen

DATE-ISSUED: July 31, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Baillie, Leslie W J	Salisbury			GB

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE	CODE
The Secretary of State for Defence	Farnborough			GB		03

APPL-NO: 09/ 242846 [PALM]

DATE FILED: February 25, 1999

PARENT-CASE:

This application is a national stage application of PCT/GB97/02288, filed Aug. 26, 1997.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
GB	9618107	August 30, 1996

PCT-DATA:

APPL-NO	DATE-FILED	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
PCT/GB97/02288	August 26, 1997	WO98/08952	Mar 5, 1998	Feb 25, 1999	Feb 25, 1999

INT-CL: [07] A61 K 39/295

US-CL-ISSUED: 424/200.1; 424/93.46, 424/93.462, 424/184.1, 424/235.1, 424/236.1, 435/69.3, 435/252.3, 435/252.31, 435/320.1, 435/480, 435/485, 530/825, 536/23.7

US-CL-CURRENT: 424/200.1; 424/184.1, 424/235.1, 424/236.1, 424/93.46, 424/93.462, 435/252.3, 435/252.31, 435/320.1, 435/480, 435/485, 435/69.3, 530/825, 536/23.7

FIELD-OF-SEARCH: 424/93.46, 424/93.462, 424/184.1, 424/200.1, 424/235.1, 424/236.1, 435/69.3, 435/252.3-252.31, 435/320.1, 435/480, 435/485, 530/300, 530/350, 530/806, 530/825, 536/23.7

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

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<i>DB=USPT; PLUR=YES; OP=AND</i>			
<u>L11</u>	anthrax adj antibodies	0	<u>L11</u>
<u>L10</u>	L9 and anthracis	3	<u>L10</u>
<u>L9</u>	((424/130.1)!.CCLS.)	764	<u>L9</u>
<u>L8</u>	L7 and antibody	30	<u>L8</u>
<u>L7</u>	((424/246.1)!.CCLS.)	46	<u>L7</u>
<u>L6</u>	L5 and bacillus	4	<u>L6</u>
<u>L5</u>	s ea1	253	<u>L5</u>
<u>L4</u>	L3 and ea1	0	<u>L4</u>
<u>L3</u>	L2 and anthracis	79	<u>L3</u>
<u>L2</u>	L1 and antibodies	227	<u>L2</u>
<u>L1</u>	anthrax	419	<u>L1</u>

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L3: Entry 59 of 79

File: USPT

Nov 24, 1998

US-PAT-NO: 5840312

DOCUMENT-IDENTIFIER: US 5840312 A

TITLE: Recombinant Bacillus anthracis strains unable to produce the lethal factor protein or edema factor protein

DATE-ISSUED: November 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mock; Michele	Paris			FR
Cataldi; Angel	Buenos Aires			AR
Pezard; Corinne	Paris			FR

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Institut Pasteur	Paris Cedex			FR	03

APPL-NO: 08/ 325647 [PALM]

DATE FILED: October 19, 1994

PARENT-CASE:

This application is a Continuation of application Ser. No. 07/961,914, filed on Mar. 2, 1993, now abandoned.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
FR	91 05417	May 2, 1991

INT-CL: [06] A61 K 39/07, C12 N 15/31, C12 N 15/75, C12 N 15/70

US-CL-ISSUED: 424/200.1; 435/69.3, 435/320.1, 435/172.3, 435/252.31, 424/93.46, 424/235.1, 424/246.1, 536/23.7

US-CL-CURRENT: 424/200.1; 424/235.1, 424/246.1, 424/93.46, 435/252.31, 435/320.1, 435/480, 435/485, 435/69.3, 536/23.7

FIELD-OF-SEARCH: 435/67.3, 435/320.1, 435/172.3, 435/252.31, 424/93.46, 424/200.1, 424/235.1, 424/246.1, 536/23.7

PRIOR-ART-DISCLOSED:

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
2181435	April 1987	GB	
90/11688	October 1990	WO	

OTHER PUBLICATIONS

Burgess et al. The Journal of Cell Biology 111:2129-2137, Nov. 1990.
Lazar et al. Molecular and Cell Biology 8(3):1247-1252, Mar. 1988.
World Patent Index Latest, Week 9042, Derwent Publications Ltd., London, GB, AN 90-319062 {42} & SU, A, 1,551,382 (Kish Medicine Inst) Mar. 23, 1990.
Infection and Immunity, vol. 54, No. 2, 1986, Washington, D.C., US, Ivins BE. et al: "Cloning and Expression of the Bacillus-anthraxis Protective Antigen Gene in Bacillus-subtilis", pp. 537-542.
Infection and Immunity, vol. 59, No. 10, 1991, Washington, D.C., US, Pezard C. et al: "Contribution of Individual Toxin Components to Virulence of Bacillus-anthraxis", pp. 3472-3477.
Molecular Microbiology, vol. 4, No. 7, 1990, New York, US, Cataldi et al: "Construction and Characterization of a Protective Antigen-Deficient Bacillus anthracis strain", pp. 1111-1117.
Toxline Database, Bethesda, MD, US, Ivins BE.: "Search for a New-Generation Human Anthrax Vaccine" abstract NTIS/AD-A190 178-4 & Govt Reports Announcements & Index, Issue 14, 1988.
Biosis Previews Database, Biosis, Philadelphia, PA, US, Singh Y. et al: "A Deleted Variant of Bacillus anthracis Protective Antigen is Non-Toxic and Blocks Anthrax Toxin Action in Vivo", abstract No. 89025806, & J. Biol. Chem., 264,32, 1989, 19103-7.

ART-UNIT: 187

PRIMARY-EXAMINER: Caputa; Anthony C.

ATTY-AGENT-FIRM: Oblon, Spivak, McClelland, Maier & Neustadt, P.C.

ABSTRACT:

A recombinant strain of B. anthracis is characterized in that it can induce the production of protective antibodies against virulent strains of B. anthracis in a human or animal host, and characterized also by the mutation of the pX01 plasmid of at least one given gene coding for a protein which causes a toxic effect of B. anthracis, wherein said mutation leads to the deletion of all or part of said gene which codes for the protein causing the toxic effect, and to the insertion of a DNA cassette at said gene's deletion site in pX01, whereby the strain thereby modified may be selected and a back mutation of the recombinant strain may be prevented, and wherein the gene thereby mutated is thereafter either unable to produce the protein causing the toxic effect for which it codes, or able to code for a truncated protein which has lost its toxic properties. The use of such a strain in immunogenic compositions is also described.

36 Claims, 6 Drawing figures

WEST☐ **Generate Collection** **Print**

L3: Entry 66 of 79

File: USPT

Oct 14, 1997

US-PAT-NO: 5677274

DOCUMENT-IDENTIFIER: US 5677274 A

**** See image for Certificate of Correction ****TITLE: Anthrax toxin fusion proteins and related methods

DATE-ISSUED: October 14, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leppla; Stephen H.	Bethesda	MD		
Klimpel; Kurt R.	Gaithersburg	MD		
Arora; Naveen	Delhi			IN
Singh; Yogendra	Delhi			IN
Nichols; Peter J.	Welling Kent			GB

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE	CODE
The Government of the United States as represented by the Secretary of	Washington DC					06

APPL-NO: 08/ 082849 [PALM]

DATE FILED: June 25, 1993

PARENT-CASE:

This application is in a continuation in part application of Ser. No. 08/021,601 filed Feb. 12, 1993 now U.S. Pat. No. 5,591,631.

INT-CL: [06] A61 K 39/00

US-CL-ISSUED: 514/2

US-CL-CURRENT: 514/2

FIELD-OF-SEARCH: 514/2, 424/1.69

PRIOR-ART-DISCLOSED:

OTHER PUBLICATIONS

Klimpel et al, "Modified Anthrax Toxin is Cleaved . . . by HIV-1 Protease" J. Cell. Biochem, Suppl. 18B:163, abstract J515 (Jan. 1994).
Friedlander, "Macrophages are Sensitive to Anthrax Lethal Toxin . . . " J. Biol. Chem. 261(16):7123-7126 (Jun. 1986).
Arora et al., J. Bio. Chem., 267(22):15542-15548 (1992).
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Quinn et al., J. Bio. Chem., 266(30):20124-20130 (1991).
Oeltmann and Frankel, News, 5:2334-2337 (Jul. 1991).
Singh et al., J. Bio. Chem., 266(23):15493-15497 (1991).
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Klimpel et al. Abstract: 1992 ASM General Meeting, New Orleans, LA (May 1992).

Novak, J.M., et al., "Functional Characterization of Protease-treated *Bacillus anthracis* Protective Antigen," J. of Biological Chemistry, 267(24):17186-17193 (Aug. 25, 1992).

Ivins, B.E., et al., "Cloning and Expression of the *Bacillus anthracis* Protective Antigen Gene in *Bacillus subtilis*," Infection and Immunity, 54(2):537-542 (Nov. 1986).

Molloy, S.S., et al., "Human Furin is a Calcium-dependent Serine Endoprotease That Recognizes the Sequence Arg-X-X-Arg and Efficiently Cleaves *Anthrax* Toxin Protective Antigen," J. of Biological Chemistry, 267(23):16396-16402 (Aug. 15, 1992).

Zhang, L., et al., "Inhibition of HIV-1 RNA Production by the Diphtheria Toxin-Related IL-2 Fusion Proteins DAB.sub.486 IL-2 and DAB.sub.389 IL-2," J. of Acquired Immune Deficiency Syndromes, 5(12):1181-1187 (1992).

O'Hare, M., et al., "Cytotoxicity of a recombinant ricin-A-chain fusion protein containing a proteolytically-cleavable spacer sequence," FEBS Lett. 273(1,2):200-204 (Oct. 1990).

Williams, D.P., et al., "Cellular Processing of the Interleukin-2 Fusion Toxin DAB.sub.486 -IL-2 and Efficient Delivery of Diphtheria Fragment A to the Cytosol of Target Cells Requires Arg.sup.194," J. of Biological Chemistry, 265(33):20673-20677 (Nov. 25, 1990).

Ohishi, I., et al., "Visualizations of Binding and Internalization of Two Nonlinked Protein Components of Botulinum C.sub.2 Toxin in Tissue Culture Cells," Infection and Immunity, 60(11):4648-4655 (Nov. 1992).

Arora, Navene., et al. (1992) "Potent hybrid cytotoxins of *anthrax* lethal factor and the ADP-ribosylation domain of *Pseudomonas* exotoxin A are translocated direct to the cytosol of mammalian cells", Abstracts of the General Meeting of the American Society for Microbiology, abstract n. B-33.

Cataldi, Angel, et al. (1992) "Regulation of pag gene expression in *Bacillus anthracis*: Use of a pag-lacZ transcriptional fusion", FEMS Microbiology Letters, 98(1-3):89-94.

Klimpel, Kurt R., et al. (1992) "*Anthrax* toxin protective antigen is activated by a cell surface protease with the sequence specificity and catalytic properties of furin", Proceedings of the National Academy of Sciences of USA, 89(21):10277-10281.

Arora, Navene, et al. (1993) "Residues 1-254 of *anthrax* toxin lethal factor are sufficient to cause cellular uptake of fused polypeptides", Journal of Biological Chemistry, 268(5):3334-3341.

ART-UNIT: 181

PRIMARY-EXAMINER: Jagannathan; Vasu S.

ASSISTANT-EXAMINER: Romeo; David S.

ATTY-AGENT-FIRM: Townsend and Townsend and Crew

ABSTRACT:

The present invention provides a nucleic acid encoding a fusion protein comprising a nucleotide sequence encoding the *anthrax* protective antigen (PA) binding domain of the native *anthrax* lethal factor (LF) protein and a nucleotide sequence encoding an activity inducing domain of a second protein. Also provided is a nucleic acid encoding a fusion protein comprising a nucleotide sequence encoding the translocation domain and LF binding domain of the native *anthrax* PA protein and a nucleotide sequence encoding a ligand domain which specifically binds a cellular target. Proteins encoded by the nucleic acid of the invention, vectors comprising the nucleic acids and hosts capable of expressing the protein encoded by the nucleic acids are also provided. A composition comprising the PA binding domain of the native LF protein chemically attached to a non-LF activity inducing moiety is further provided. A method for delivering an activity to a cell is provided. The steps of the method include a) administering to the cell a protein comprising the translocation domain and the LF binding domain of the native PA protein and a ligand domain, and b) administering to the cell a product comprising the PA binding domain of the native LF protein and a non-LF activity inducing moiety, whereby the product administered in

step b) is internalized into the cell and performs the activity within the cell. The invention also provides proteins including an anthrax protective antigen which has been mutated to replace the trypsin cleavage site with residues recognized specifically by the HIV-1 protease.

12 Claims, 1 Drawing figures

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L6: Entry 1 of 4

File: USPT

Feb 13, 2001

US-PAT-NO: 6187533

DOCUMENT-IDENTIFIER: US 6187533 B1

**** See image for Certificate of Correction ****

TITLE: Mutations in the diabetes susceptibility genes hepatocyte nuclear factor (HNF) 1 alpha (.alpha.), HNF1.beta. and HNF4.alpha.

DATE-ISSUED: February 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bell; Graeme I.	Chicago	IL		
Yamagata; Kazuya	Kaizuka			JP
Oda; Naohisha	Chicago	IL		
Kaisaki; Pamela J.	Headington			GB
Furuta; Hiroto	Wakayama			JP
Horikawa; Yukio	Chicago	IL		
Menzel; Stephan	Headington			GB

US-CL-CURRENT: 435/6; 435/91.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC
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☐ 2. Document ID: US 5885831 A

L6: Entry 2 of 4

File: USPT

Mar 23, 1999

US-PAT-NO: 5885831

DOCUMENT-IDENTIFIER: US 5885831 A

TITLE: Nuclear localization factor associated with circadian rhythms

DATE-ISSUED: March 23, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Young; Michael W.	Upper Saddle River	NJ		
Sehgal; Amita	Haverford	PA		
Vosshall; Leslie B.	New York	NY		
Price; Jeffrey L.	Morgantown	WV		
Myers; Michael P.	Washington Township	NJ		

US-CL-CURRENT: 435/336; 435/252.33, 530/350, 530/388.24, 536/24.31

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC
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☐ 3. Document ID: US 5436150 A

L6: Entry 3 of 4

File: USPT

Jul 25, 1995

US-PAT-NO: 5436150

DOCUMENT-IDENTIFIER: US 5436150 A

TITLE: Functional domains in flavobacterium okeanokoities (foki) restriction endonuclease

DATE-ISSUED: July 25, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chandrasegaran; Srinivasan	Baltimore	MD		

US-CL-CURRENT: 435/199; 435/252.33, 435/69.7, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMIC
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☐ 4. Document ID: US 5356802 A

L6: Entry 4 of 4

File: USPT

Oct 18, 1994

US-PAT-NO: 5356802

DOCUMENT-IDENTIFIER: US 5356802 A

**** See image for Certificate of Correction ****

TITLE: Functional domains in flavobacterium okeanokoites (FokI) restriction endonuclease

DATE-ISSUED: October 18, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Chandrasegaran; Srinivasan	Baltimore	MD		

US-CL-CURRENT: 435/199; 536/23.2, 536/23.4

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMIC
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L10: Entry 1 of 3

File: USPT

Oct 29, 2002

US-PAT-NO: 6471968

DOCUMENT-IDENTIFIER: US 6471968 B1

TITLE: Multifunctional nanodevice platform

DATE-ISSUED: October 29, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Baker, Jr.; James R.	Ann Arbor	MI		
Tomalia; Donald A.	Ann Arbor	MI		

US-CL-CURRENT: 424/280.1; 424/1.11, 424/130.1, 424/277.1, 424/94.1, 514/44, 536/23.1, 536/24.1, 536/24.5

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KIMC
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☐ 2. Document ID: US 6270777 B1

L10: Entry 2 of 3

File: USPT

Aug 7, 2001

US-PAT-NO: 6270777

DOCUMENT-IDENTIFIER: US 6270777 B1

TITLE: Conserved metalloprotease epitopes

DATE-ISSUED: August 7, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sokol; Pamela A.	Calgary			CA
Kooi; Cora D.	Calgary			CA

US-CL-CURRENT: 424/260.1; 424/130.1, 424/184.1, 424/185.1, 424/190.1, 424/197.11, 424/234.1, 424/246.1, 424/261.1, 424/94.67, 530/300, 530/324, 530/325, 530/326, 530/327, 530/328, 530/350, 530/387.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KIMC
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☐ 3. Document ID: US 5904922 A

L10: Entry 3 of 3

File: USPT

May 18, 1999

US-PAT-NO: 5904922

DOCUMENT-IDENTIFIER: US 5904922 A

TITLE: Treatment with polyvalent antivenom containing immunoglobulin which is greater than 50% venom-reactive

DATE-ISSUED: May 18, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Carroll; Sean B.	Cottage Grove	WI		

US-CL-CURRENT: 424/130.1; 424/158.1, 424/542, 435/174, 435/178, 435/180, 436/518, 436/529, 436/824, 514/2, 514/21, 530/387.1, 530/389.1, 530/413, 530/810, 530/813, 530/856, 530/858

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMC
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Long et al. J. Applied Microbiology. 1999. 87(2). page 214-?. send entire document.

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AU 1645

PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
<input type="checkbox"/> 5591631	January 1997	Leppla et al.	435/252.3

OTHER PUBLICATIONS

Baillie et al. Evaluation of *Bacillus subtilis* strain IS53 for the production of *Bacillus anthracis* protective antigen. Letters in Applied Microbiology. vol. 19 (1994) pp. 225-227.*

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Riffkin et al. A single amino-acid change between the antigenically different extracellular serine protease V2 and B2 from *Dichelobacter nodusus*. Gene. vol. 167 (1995) pp. 279-283.*

Ivins Be et al: "Cloning and expression of the *Bacillus anthracis* protective antigen gene in *Bacillus subtilis*." Infect Immun, Nov. 1986, 54 (2) P537-42, United States, SP002049155 see whole document.

Miwa Y et al: "Determination of the CIS Sequence Involved in Catabolite Repression of the *Bacillus-Subtilis* GNT Operon Implication of a Consensus Sequence in Catabolite Repression in the Genus *Bacillus*" Nucleic Acids Research, 18 (23). 1990. 7049-7054., xp002049156 see whole document.

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Strauch Ma: "AbrB modulates expression and catabolite repression of a *Bacillus subtilis* ribose transport operon." J Bacterio, Dec. 1995, 177 (23) P6727-31, United States, XP002049153 see the whole document.

Huect CJ et al: "Analysis of a CIS-Active Sequence Mediating Catabolite Repression in Gram-Positive Bacteria" Research In Microbiology, 1994, 145, 503-518, XP002049154 see whole document.

ART-UNIT: 168

PRIMARY-EXAMINER: Stucker; Jeffrey

ASSISTANT-EXAMINER: Winkler; Ulrike

ATTY-AGENT-FIRM: Nixon & Vanderhye P.C.

ABSTRACT:

Methods of preparing recombinant *Bacillus anthracis* protective antigen or a variant or fragment thereof for use in vaccines is disclosed. The protein is expressed in a recombinant microorganism which comprises a sequence which encodes PA or said variant or fragment thereof wherein either (i) a gene of the microorganism which encodes a catabolic repressor protein and/or AbrB is inactivated, and/or (ii) wherein a region of the PA sequence which can act as a catabolic repressor binding site and/or an AbrB binding site is inactivated. Useful quantities of protein are obtainable from these organisms.

33 Claims, 3 Drawing figures